Claims

1. A method of performing a non-invasive measurement of a target analyte present in a patient's blood or tissue, the method comprising the steps of:

compiling a database of spectral measurements for a plurality of subjects, the spectral measurements being taken transdermally by utilizing light,

orthogonalizing the spectral measurements to a known chromophore measured in each of the subjects, thereby producing a set of orthogonalized spectral measurements, and

deriving spectral shapes corresponding to one or more variability factors based on said orthogonalized spectral measurements.

2. The method of claim 1, further comprising the step of collecting calibration spectra with variation in the target analyte.

3. The method of claim 2, further comprising the step of utilizing the derived spectral shapes to correct the collected calibration spectra.

4. The method of claim 2, further comprising the step of generating a calibration model based on said corrected calibration spectra.

5. The method of claim 1, wherein the orthogonal spectral measurements are coordinatized, and the step of deriving spectral shapes includes the step of applying a multivariate calibration technique to a coordinate.

6. The method of claim 4, wherein said variability factor is selected to represent variability in any of skin color, fat content derived from body mass index (BMI), fat content derived from body surface area (BSA), age or a disease condition among the subjects.

7. The method of claim 5, wherein the coordinate includes one or more of L, **a**, **b**, hue and chroma and a function thereof.

8. The method of claim 4, wherein the coordinate is luminance in a CIE L*a*b spectral representation.

9. The method of claim 7, wherein the coordinate is a coordinate in a CIE L*a*b spectral representation or a quantity calculated from one or more said coordinates.

10. The method of claim 1, wherein said at least one spectral shape is applied to normalize a set of spectral data forming a calibration model for a target analyte to thereby enhance accuracy of *in vivo* spectral detection of the target analyte.

11. The method of claim 1, wherein said variability factor is selected to represent variability inherent in measurement process.

12. The method of claim 4, further comprising the steps of:

collecting one or more new transdermally obtained spectra from a group of subjects unrelated to the subjects employed for compiling the database,

correcting the new spectra based on the derived spectral shapes, and

applying the calibration model to the new corrected spectra to measure the target analyte.

13. A method of performing a non-invasive measurement of a target analyte present in a subject's blood or tissue, comprising:

compiling a database of transdermally collected spectral measurements for a plurality of subjects,

deriving spectral shapes corresponding to one or more human contributing factors from said collected spectra, and

normalizing the collected spectra based on the derived spectral shapes to generate a set of corrected spectra.

14. The method of claim 12, wherein said variability factor represents variability in any of skin color, fat content derived from body mass index (BMI), fat content derived from body surface area (BSA), age, and disease condition.

15. The method of claim 12, further comprising the step of enhancing a calibration model based on said corrected spectra for measuring the target analyte.

16. The method of claim 12, wherein said human contributing factors are selected to be any of skin color, fat content, or cell scattering.

17. A method of performing a non-invasive measurement of a target analyte present in a subject's blood or tissue, comprising:

compiling a database of transdermally obtained spectra for a plurality of subjects,

deriving spectral shapes corresponding to one or more human contributing factors from said transdermally obtained spectra,

normalizing the transdermally obtained spectra based on the derived spectral shapes to generate a set of corrected spectra, and

utilizing the corrected spectra to augment a calibration model.

18. A spectrometer for *in vivo* analysis of a target analyte present in a subject's blood or tissue, comprising

a light source and a light collector for, respectively, illuminating and collecting light from the subject's tissue and/or blood to provide a transdermal tissue spectrum, and

a processor operative on the spectrum to measure the target analyte,

wherein said processor operates with a calibration model based on a set of spectra obtained from a group of subjects having variable analyte concentrations and normalized by one or more spectral shapes indicative of one or more human variability factors.

19. The spectrometer of claim 18, further comprising a wavelength dispersing element coupled to the light collector for obtaining the tissue spectrum.

20. The spectrometer of claim 18, wherein the human variability factors can be any of skin color, fat content, age or disease condition.

21. A spectrometer for *in vivo* analysis of a target analyte, said spectrometer including a light source and light collector for illuminating and collecting light from tissue, and a processor operative on the collected light, wherein said processor operates to correct collected spectra with a transformation determined from spectral measurements taken in a selected population group, wherein the selected population group is a group selected to model spectral contribution of a human contributing factor, thereby enhancing detection of the target analyte in the presence of said human contributing factor.